

REMARKS

Attached hereto is a marked-up version of the changes made to the specification by the above amendment. The attached page is captioned **“Version with markings to show changes made.”**

The amendments to claim 15 does not alter the scope of the claims but merely recites the underlying characteristics of “fast breaking” and “rapid release” liposomes already present in the claims via claim 15 as originally presented. Additional support for the inclusion of “osmolarity of the liposomes” is provided at least on page 10, first full paragraph, and Examples 2 and 3.

The amendment to claim 27 corrects a grammatical error that was detected upon further review of the claim.

Support for new claims 33 and 34 is provided at least by original claim 5 as filed, the bottom of page 10, and page 13, lines 1-6.

The amendments are made for reasons relating to business considerations and commercial embodiments of the invention rather than issues of patentability. No new matter has been added and entry of the amendment is respectfully requested.

Before addressing the Office Action in detail, Applicants respectfully point out that the present invention is directed to liposomal formulations of porphyrin macrocycle photosensitizers that are “fast breaking” such that they rapidly deliver the photosensitizers into the lipoprotein compartment of blood. As such, they must have inherent characteristics that are conferred by the combination of phospholipids and sugars present in the formulations. Stated differently, not all

formulations composed of phospholipids and sugars have the characteristics of those of the claimed invention.

Rejection under obviousness type double patenting

Claims 15-32 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of USP 6,074,666.

Applicants thank the Examiner for indicating that this rejection will be held in abeyance until the claims are found to be otherwise allowable.

Rejection under 35 U.S.C. § 102(e)

Claims 15-20 and 30-32 have been rejected under 35 U.S.C. § 102(e) over Madden (USP 5,389,378). Applicants have carefully reviewed the reference and the statement of the rejection and respectfully traverse because no *prima facie* case of anticipation has been presented.

The position set forth in this rejection appears to be that the “instant claims are composition claims and Madden teaches the same compositions....” Applicants respectfully traverse because contrary to the view as indicated in the above quote, Madden does not teach the preparation of any actual liposomal formulation comprising sugar (see Examples 1-6 therein).

The instant claims, however, all require the inclusion of sugar, whether a disaccharide, monosaccharide, or a polysaccharide. Moreover, the instant claims require that the claimed formulations have the osmolarity of human blood (about 300 mosm/L) which results from particular ranges of sugar present in the formulations (see for example Examples 1A to 1F of the instant application). Because Madden fails to teach any formulation having the sugar, and thus osmolarity, of the claimed invention, Madden cannot anticipate the instant invention.

Applicants respectfully request this rejection be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 15-20 and 26-32 have been rejected under 35 U.S.C. § 103(a) over Thompson et al. (USP 5,277,913) or Kappas et al. (USP 5,010,073) individually in view of Crowe et al. (USP 4,857,319). Applicants have carefully reviewed the references and the statement of the rejection and respectfully traverse because no *prima facie* case of obviousness has been presented.

The statement of the rejection acknowledges that neither Thompson or Kappas teach liposomal formulations that comprise sugar and that Crowe rectifies this deficiency.

Applicants point out, however, that Crowe teaches the inclusion of sugar to protect liposomes during dehydration and rehydration, *which are not co-terminus with producing an osmolarity similar to that of human blood.*

All three of the cited references are completely silent on the concept of osmolarity and the advantageous property of “fast-breaking” and rapid release of photosensitizer that is associated therewith when liposomes have the osmolarity of human blood due to the combinations of phospholipids and sugar as disclosed by the instant application. Because none of the references provide any guidance or suggestion as to particular combinations of phospholipids and sugar to arrive at the claimed invention, there would have been no motivation for the artisan of ordinary skill to modify the teachings of the cited references to arrive at the claimed invention. Absent such motivation, and contrary to the assertion in the statement of the rejection, the claimed invention must be non-obvious.

Applicants respectfully submit that the notions that “ratios are manipulatable parameters” and that demonstration of “criticality” is necessary raise no issues because the claims are directed

to formulations that are not taught or suggested by some undefined “manipulation” of the phospholipid and sugar combinations taught by the cited references, alone or in combination. Applicants therefore respectfully request that the instant rejection be withdrawn.

Claims 15-32 have been rejected under 35 U.S.C. § 103(a) over Madden (USP 5,389,378) or Thompson et al. (USP 5,277,913) or Kappas et al. (USP 5,010,073) individually in view of Crowe et al. (USP 4,857,319). Applicants have carefully reviewed the references and the statement of the rejection and respectfully traverse because no *prima facie* case of obviousness has been presented.

The statement of the rejection appears to be based upon the notion that the modifications of the cited references to arrive at the claimed invention is based on “the expectation of obtaining similar results” and that “one would expect the liposomes to act the same way irrespective of the type of porphyrin used”. As noted above, none of Thompson, Kappas, or Crowe teach or suggest anything related to the osmolarity related “fast-breaking” and rapid photosensitizer release features of the claimed invention. Madden is also completely silent in this aspect.

Therefore, Applicants respectfully submit that no combination of the cited references can result in the claimed invention because there is simply no teaching or suggestion that would lead to the formulations as claimed. There is nothing in the cited references that would lead to the combination of phospholipids and sugars to result in liposomes that rapidly release photosensitizer.

In light of these deficiencies, Applicants thus respectfully request that the instant rejection be withdrawn.

Conclusion

In light of the above discussion, Applicants respectfully submit that the claims are allowable, and passage of the application to issue is urged. The Examiner is welcome to contact the undersigned to resolve any residual issues, such as the submission of a terminal disclaimer, or if further discussions may be thought useful.

In the event that the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **273012008102**. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

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Version with markings to show changes made.

Kindly amend the claims as follows:

15. (twice amended) A liposomal formulation comprising liposomes that comprise a porphyrin macrocycle photosensitizer, phospholipids and one or more sugars, wherein the osmolarity of the liposomes is that of human blood and wherein said liposomes are fast breaking and rapidly release the photosensitizer into the bloodstream to associate with lipoproteins upon in vivo administration.

27. (amended) The liposomal formulation of claim 26 wherein the amount of sugar, relative to said amounts of photosensitizer, dimyristoyl phosphatidyl choline, and egg phosphatidyl glycerol in said liposomes on a per weight basis, is about 8.0 to 12.0 of sugar when said sugar is a disaccharide, or about half that amount if said sugar is a monosaccharide.